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CROWELL & MORING LLP
INTELLECTUAL PROPERTY GROUP
P.O. BOX 14300
WASHINGTON, DC 20044-4300

EXAMINER	
JONES, DAMERON LEVEST	
ART UNIT	PAPER NUMBER
1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/084,674	BARTHOLOMAEUS ET AL.	
	Examiner	Art Unit	
	D. L. Jones	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/21/03; 6/19/07; & 2/19/08*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-67* is/are pending in the application.

4a) Of the above claim(s) *10,13,14,16,20,22-29,33-54 and 59-61* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-9,11,12,15,17-19,21,30-32,55-58 and 62-67* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 February 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

CLARIFICATION OF RECORD

1. It is duly noted in the decision from the panel regarding the pre-appeal brief review mailed 2/19/08 that prosecution would be reopened and the rejection withdrawn.

Note: In Applicant's pre-appeal brief filed 12/11/07, it is noted that Applicant did not rebut the 102 rejection, only the 102 rejection. However, since it is unclear if the pre-appeal panel agreed to withdraw this rejection as well, the current Examiner has reviewed this document and deemed that the 102 rejection should be withdrawn as well.

ACKNOWLEDGMENTS

2. The Examiner acknowledges receipt of the amendment filed 6/19/07 wherein claim 2 was canceled and claim 1 was amended.

Note: Claims 1 and 3-67 are pending.

APPLICANT'S INVENTION

3. Applicant's invention is directed to controlled release oral dosage formulations comprising a salt forming active ingredient that is present in at least two different salts in a solid aggregation as set forth in independent claim 1.

APPLICANT'S ELECTION

4. Applicant's provisional election of the species wherein tramadol and diclofenac are the active ingredients, the dosage form is a tablet, the matrix material is ethyl cellulose, and the sustained release formulation is achieved by using a retarding matrix is acknowledged in Applicant response filed 7/21/03. It is noted that no traversal was provided as to why the election of species was not proper. Hence, the election is deemed proper and is therefore made FINAL.

Note: *The search was not expanded beyond Applicant's elected species because prior art was found which could be used to reject the claims.*

WITHDRAWN CLAIMS

5. Claims 10, 13, 14, 16, 20, 22-29, 33-54, and 59-61 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention/species.

DOUBLE PATENTING REJECTION

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In *re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory

double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 3-9, 11, 12, 15, 17-19, 21, 30-32, 55-58, 62, 63, 65, and 67 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of U.S. Patent No. 6,558,701. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to two different active agents (tramadol and diclofenac) in a tablet. The claims differ in that those of the instant invention are not limited to tramadol and diclofenac (Applicant's elected species). However, a skilled artisan would recognize that the claims of the instant invention encompass the subject matter of the patented invention.

8. Claims 1, 3-9, 11, 12, 15, 17-19, 21, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-19 of copending Application No. 10/837,755. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a formulation comprising tramadol and a pharmaceutically acceptable acidic substance. The claims differ in that those of the instant invention are

not limited to tramadol (this is one of the Applicant's elected species) and both application disclose that an acidic substance which may be diclofenac in both cases is present. Thus, a skilled artisan would recognize that both applications encompass overlapping subject matter since they both read on a formulation comprising tramadol and diclofenac.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

9. Claims 1, 3-9, 11, 12, 15, 17-19, 21, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-28 of copending Application No. 10/665,552. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a formulation comprising tramadol and diclofenac. The claims differ in that the instant invention is not limited to any particular combination (the tramadol and diclofenac formulation is Applicant's elected species). Hence, the skilled artisan would recognize that the claims of the instant invention encompass those of 10/665,552.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

10. Claims 1, 3-9, 11, 12, 15, 17-19, 21, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over

claims 1-28 of copending Application No. 10/016,130. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a formulation comprising tramadol and diclofenac. The claims differ in that the instant invention is not limited to any particular combination (the tramadol and diclofenac formulation is Applicant's elected species). Hence, the skilled artisan would recognize that the claims of the instant invention encompass those of 10/016,130.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims 1, 3-9, 11, 12, 15, 17-19, 21, and 30-32 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-25 of copending Application No. 10/084,676. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to a formulation comprising tramadol and a pharmaceutically acceptable acidic substance. The claims differ in that those of the instant invention are not limited to tramadol (this is one of the Applicant's elected species) and both application disclose that an acidic substance which may be diclofenac in both cases is present. Thus, a skilled artisan would recognize that both applications encompass overlapping subject matter since they both read on a formulation comprising tramadol and diclofenac.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

112 FIRST PARAGRAPH REJECTIONS

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claim 5 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims lack written description because they were not described in such a manner that the item to be patented is clear to the Reader to ensure that the Inventor actually had possession and knowledge of the unique composition that makes it worthy of patent protection at the time of application filing. In particular, the terms appearing in claim 5 encompass a multitude of possible active ingredients for which specific active ingredients encompassed by those broad groups (i.e., detoxification drugs, circulation stimulating drugs, broncholytics, corticoids for internal administration geriatric drugs, gout treatment drugs, regulatory peptides, regulatory peptide inhibitors, cardiac drugs, analeptics, immunomodulators, diuretics, enzymes, fungistatics, hormones, lipid lowering drugs, gastrointestinal drugs, etc.) are not described in the specification

112 SECOND PARAGRAPH REJECTIONS

14. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claim 5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claim as written is ambiguous because it is unclear what specific active ingredients that are encompassed by the phrases of claim 5 (e.g., slimming drugs, drugs for treatment of acidosis, drugs for treatment of vertigo, geriatric drugs, gout treatment drugs, hypothalamic hormones, regulator peptides, muscle relaxants, vein therapeutics, antineoplastic protectives, virustatics, tonics, roborants, etc.) that Applicant is/are claiming to be compatible with the instant invention. In addition the phrase 'muscle relaxants' appears in the claim twice (see lines 21 and 27).

103 REJECTIONS

16. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

17. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

18. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

19. Claims 1, 3-9, 11, 12, 15, 17, 18, 19, 21, 30-32, 55-58, 62-65, and 67are rejected under 35 U.S.C. 103(a) as being unpatentable over Krishnamurthy (US Patent No. 5,811,126) in view of Gruber (US Patent No. 6,709,678) in further view of Oshlack et al (WO 99/01111).

Krishnamurthy discloses a controlled release pharmaceutical composition for oral administration (see entire document, especially, abstract). The dosage form for the controlled release of an orally administered substance includes a pharmaceutically acceptable swellable polymer and a pharmaceutically acceptable divalent salt. A therapeutically active agent is used with the polymer and divalent salt to product tablets (columns 3, lines 34-47). The water swellable polymer may be a cellulose ether or a

substituted or unsubstituted polymer such as a hydroxyalkycellulose, hydroxyethylcellulsoe, hydropropylcellulose, and/or a carboxyalkylcellulose (column 3, lines 48-56). Any therapeutically active agent/drug or diagnostic agent may be incorporated into the composition of the invention. Possible therapeutically active agents may include a combination of diclofenac or tramadol (Column 4, lines 34-44). The composition may be coated (column 4, lines 46-54). The controlled release matrix of Krishnamurthy provides superior controlled release characteristic upon oral ingestion and contact with fluids (column 5, lines 34-40). The amount of divalent salt is sufficient to crosslink the alginate when exposed to a solution such as the gastric fluids (column 6, lines 55-62). The solid dosage form of Krishnamurthy may be prepared in any suitable form for oral administration including as a tablet (column 7, lines 5-9). Krishnamurthy fails to specifically disclose a formulation containing tramadol and diclofenac present in the solid aggregation state. However, Krishnamurthy discloses that it multiple drugs such as tramadol and diclofenac may be present in the solid administration which is eventually coated for various reasons. In addition, Krishnamurthy fails to disclose various possible hydrophilic matrix combinations useful with their invention.

Gruber discloses oral compositions which may be dispersed in an aqueous carrier (see entire document, especially, abstract). The pharmaceutical composition for oral administration may comprise ***at least one pharmaceutically active compound*** in an effective amount and comprising one or more coated particles (column 1, lines 6-11; column 9, lines 51-52). In particular, the composition may be in the form of a tablet

(column 5, lines 10-16). Possible active ingredients that may be present in the compositions include diclofenac and tramadol (column 5, lines 51 and 52; column 6, line 29). Natural and semi-synthetic polymers may be used with the compositions. Possible polymers include cellulose ethers such as methylcellulose, hydroxyethylcellulose, hydroxypropylcellulose, and hydroxypropylmethyl cellulose. Other polymers include polyacrylic acids, polyacrylates, methacrylic acid, and ammonium methacrylate copolymer (column 7, lines 3-5 and 8-9; column 15, lines 31-55). The tablet may be designed such that the coating layer or the outermost coating layers envelopes the pressed coated tablet (column 10, lines 23-26). Particles coated according to Gruber may also be processed further into tablets. The particles may be mixed with conventional tableting ancillary substances and compressed to tablets in a manner known in the art. However, the coated particles may be compressed into tablets without adding further ancillary substances (columns 14-15, bridging paragraph).

Oshlack et al disclose stabilized sustained release tramadol formulations in the solid dosage form (see entire document, especially, abstract; page 4, lines 11-14; page 18, lines 30-31). In order to obtain a controlled release of the active agent, the therapeutically active agent is homogeneously combined with a sufficient amount of a hydrophobic (release retardant) material which may include a hydrophobic polymer such as an water insoluble acrylic polymer (methyl methacrylate copolymers, poly(methacrylic acid), methyl methacrylate, poly(methyl methacrylate, or ammonio methacrylate copolymers) or alkylcellulose (page 11, lines 6-10; page 15, lines 13-31). Other hydrophilic polymers include hydroxypropylmethylcellulose, hydroxyalkycellulose,

and carboxyalkylcellulose (column 16, lines 4-16). The tablets may be coated with the hydrophobic material (column 6-29). Furthermore, Oshlack et al disclose that persons skilled in the art of pharmaceutical formulation are capable of altering the time and temperature necessary to reach a certain endpoint based up their varying particular ingredients and amounts of ingredients present in the formulation (page 42, lines 7-10).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the invention of Krishnamurthy using the teachings of Gruber, and Oshlack et al and generate formulations comprising a controlled release oral dosage formulation comprising an active ingredient that is present as at least two different salts in a solid aggregation for the reasons below. Krishnamurthy and Gruber disclose formulations that may comprise multiple active ingredients. Possible active ingredients included tramadol and diclofenac.

It would have been obvious to the skilled practitioner in the art to use various retarding matrices, especially one based upon a hydrophilic matrix material (i.e., cellulose) because Krishnamurthy, Gruber, and Oshlack all disclose various possible hydrophilic matrix combinations and materials. Thus, it is well known in the art to utilize various hydrophilic matrix materials in order to generate a controlled release oral formulation (i.e., tablet) for administering to a subject. Likewise, it would have been obvious to one of ordinary skill in the art at the time the invention is made to coat the formulation with various gastric juice resistant protective coatings because each document discloses that the tramadol containing formulations in the tablet form may optional comprise a coating which enables the drugs to be sustained released over a

designated period of time. Hence, a skilled artisan would be motivated to vary the coating depending on the gastric juice concentration of the subject being treated. Furthermore, based on the teachings of Krishnamurthy, Gruber, and Oshlack et al, a skilled artisan would have the tools necessary to optimize the various parameters (i.e., gastric juice resistant coating) using routine experimentation based on the prior art disclosed conditions. In particular, since the prior art documents disclose the general conditions of the coating, it is not inventive to discover the optimum or workable ranges by routine experimentation (In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)).

While neither reference specifically states that the active ingredients have different water solubility and release the active ingredient in vitro at different release rates, the skilled artisan would recognize that both tramadol and diclofenac have different chemical properties; thus, they would be expected to behave differently. Furthermore, a skilled artisan would recognize that a compound is inseparable from its properties. Hence, if both Applicant and the prior art disclose that the active ingredients are tramadol and diclofenac, they the behavior exemplified by Applicant's active ingredients would be the same as that exemplified by the prior art since both tablet compositions would contain the same ingredients.

Since all of the references disclose a formulation comprising tramadol, the reference teachings may be considered to be within the same field of endeavor. Thus, the reference teachings are combinable.

SPECIFICATION

20. The disclosure is objected to because of the following informalities: The specification does not contain the heading 'Brief Description of the Drawings' and a description of each figure.

Appropriate correction is required.

COMMENTS/NOTES

21. The Examiner is aware of numerous applications with similar subject matter. However, while an effort has been made to review all applications containing overlapping subject matter, some applications may have been missed. Thus, Applicant is respectfully requested to submit all serial numbers of applications containing overlapping subject matter for review by the Examiner.

22. Applicant is respectfully requested to correct the spelling of 'diclofenacate' throughout the disclosure. The correct spelling is 'diclofenac'.

23. Any inquiry concerning this communication or earlier communications from the examiner should be directed to D. L. Jones whose telephone number is (571) 272-0617. The examiner can normally be reached on Mon.-Fri., 6:45 a.m. - 3:15 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/D. L. Jones/

D. L. Jones
Primary Examiner
Art Unit 1618

April 21, 2008